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10/677,558	10/02/2003	Muriel Audit	1759135	8440

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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	**Application No.** 10/677,558	**Applicant(s)** AUDIT ET AL.
	Examiner Louise Humphrey, Ph.D.	**Art Unit** 1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2006*.
2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.
3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.
4a) Of the above claim(s) *15-24* is/are withdrawn from consideration.
5)☐ Claim(s) _____ is/are allowed.
6)☒ Claim(s) *1-14 and 25* is/are rejected.
7)☐ Claim(s) _____ is/are objected to.
8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.
10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a)☐ All b)☐ Some * c)☐ None of:
1.☐ Certified copies of the priority documents have been received.
2.☐ Certified copies of the priority documents have been received in Application No. _____.
3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date *10/2/03*.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant elects Group I, claims 1-14 and 25, without traverse. Claims 15-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 03 August 2006.

Information Disclosure Statement

An initialed and dated copy of each of Applicant's IDS form 1449, filed on 02 October 2003, is attached to the instant Office action.

Claim Objections

Claim 1 is objected to because it refers to two viruses by their acronyms, MLV and GaLV, without first identifying them by their full names, respectively the Moloney Murine Leukemia Virus and the Gibbons Ape Leukemia Virus.

Claim 11 is objected to because there is a ")" after the word ""ID 3-ampho-2 domain."

Appropriate correction is required.

Claim Rejections - 35 USC § 112, 2nd ¶

The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8 and 11 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 8, the phrase "the part A of the *env*" is indefinite because part A is not defined anywhere in the application.

Claim 11 is confusing in their recitation of "encodes the Env polyprotein which are located, firstly, between amino acids Nos. 1 and 31 'ID 3-ampho-1 domain' and secondly, between amino acids Nos. 645 and 676 'ID 3-ampho-2 domain' of the sequence SEQ ID NO:3," which can be interpreted in two ways: (1) the plasmid encodes two fragments of SEQ ID NO:3; the first fragment is between amino acids 1 and 31; the second fragment is between amino acids 645 and 676; or (2) the plasmid encodes amino acids 32-644 of SEQ ID No:3.

Clarification and/or correction are required.

Claim Rejections - 35 USC § 112, 1st ¶, written description

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 4, 7, 11, 13 and 25 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The factors considered in the Written Description requirement are (1) *level of skill and knowledge in the art*, (2) *partial structure*, (3) *physical and/or chemical properties*, (4) *functional characteristics alone or coupled with a known or disclosed correlation between structure and function*, and the (5) *method of making the claimed invention*. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." M.P.E.P. §2163.

For a generic claim, the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See M.P.E.P. § 2163. Although the M.P.E.P. does not define what constitutes a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad genus. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims are directed to plasmids encoding proteins of sequences exhibiting at least 70%, 80%, or 95% homology with an identified sequence, or plasmids exhibiting at least a certain % homology with an identified sequence. The limitation "a sequence exhibiting at least 70% homology with SEQ ID NO:1" encompasses all sequences with 377 (538*70%) or more amino acids identical to SEQ ID NO:1. Since there are 19 alternate amino acids that can substitute in each of the remaining 161 positions, the number of possible combinations is calculated by

$$19^{161} \times 538!/161!(538-161-1)!$$

There are approximately 4.1×10^{349} variant amino acid sequences with at least 70% identity to SEQ ID NO:1.

The limitation "a sequence exhibiting at least 80% homology with SEQ ID NO:2" encompasses all sequences with 960 (1199*80%) or more amino acids identical to SEQ ID NO:2. Since there are 19 alternate amino acids that can substitute in each of the remaining 239 positions, the number of possible combinations is calculated by

$$19^{239} \times 1199!/239!(1199-239-1)!$$

There are approximately 1.4×10^{567} variant amino acid sequences with at least 80% identity to SEQ ID NO:2.

The limitation "a sequence exhibiting at least 80% homology with SEQ ID NO:4" encompasses all sequences with 7112 (8889*80%) or more nucleotides identical to SEQ ID NO:4. Since there are 3 alternate nucleotides that can substitute in each of the remaining 1777 positions, the number of possible combinations is calculated by

$$3^{1777} \times 8889!/1777!(8889-1777-1)!$$

There are approximately 1.0×10^{2781} variant nucleotide sequences with at least 80% identity to SEQ ID NO:4.

The limitation "a sequence exhibiting at least 95% homology with SEQ ID NO:3" encompasses all sequences with 643 (676*95%) or more amino acids identical to SEQ ID NO:3. Since there are 3 alternate nucleotides that can substitute in each of the remaining 33 positions, the number of possible combinations is calculated by

3^{33} x 676!/33!(676-33-1)!

There are approximately 4.5 x 10^{74} variant amino acid sequences with at least 95% identity to SEQ ID NO:3.

Therefore, the claims are drawn to a genus of polynucleotides that are defined only by the percentage of sequence identity.

The specification only provides description for 6 of the possible sequences with at least 70% homology with SEQ ID NO:1 as recited in claim 3 (p.8, ¶32), 4 of the possible sequences with at least 80% homology with SEQ ID NO:2 as recited in claim 4 (p.9, ¶35). There are still at least 4.1x10^{349} variant amino acid sequences with at least 70% identity to SEQ ID NO:1, 1.4x10^{567} variant amino acid sequences with at least 80% identity to SEQ ID NO:2, 1.0x10^{2781} variant nucleotide sequences with at least 80% identity to SEQ ID NO:4, and 4.5x10^{74} variant amino acid sequences with at least 95% identity to SEQ ID NO:3 that are not described in the specification, let alone the shorter fragments with the % homology. Therefore, the disclosed sequences do not constitute a representative number of species to adequately describe such a broad and highly variable genus.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483, claims directed to mammalian FGF's were found to be unpatentable due to lack of written descriptions for that broad class.

Therefore, claims 3, 4, 7, 11, 13 and 25 do not meet the written description provision of 35 U.S.C. §112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variable. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 13 is rejected under 35 U.S.C. §102(b) as being anticipated by Miller *et al.* (1986, IDS No. CB).

The instant invention is a plasmid comprising the viral genome corresponding to SEQ ID NO:4 or a sequence exhibiting at least 80% homology with SEQ ID NO:4.

Miller *et al.* teach a plasmid, pAM, with hybrid amphotropic/MLV sequence (Genebank accession number AF010170), which exhibits 81.1% homology with SEQ ID NO:4. See the attached sequence alignment. Thus, the instant invention is anticipated by Miller *et al.*

Claim 25 is rejected under 35 U.S.C. §102(b) as being anticipated by Cosset *et al.* (WO200071578A2).

The instant invention is a chimeric env sequence encoding the Env protein corresponding to the amino acid sequence SEQ ID NO:3 or a sequence exhibiting at least 95% homology with SEQ ID NO:3.

Cosset *et al.* teach an Env polypeptide that exhibits 95.6% homology with SEQ ID NO:3. See Figure 17 and the attached sequence alignment. Thus, the instant invention is anticipated by Cosset *et al.*

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7 and 9-14 are rejected under 35 U.S.C. §103(a) as being unpatentable over Hu *et al.* (US 7,101,541 B2) in view of Stitz *et al.* (2000).

The instant invention is a plasmid comprising a replicative retroviral genome, where the genome comprises a psi sequence, MLV *gag* and *pol* sequences, and a chimeric *env* sequence from MLV and GaLV.

Hu *et al.* disclose a series of MLV-based retroviral vectors containing *cis*-acting *psi* packaging signal sequence, MLV *gag* and *pol* sequences, and GaLV *env* in the region of deleted MLV *env* sequence (col. 21, lines 16-20). Hu *et al.* do not disclose the chimeric *env* sequence comprising a region corresponding to MLV *env* gene and a region corresponding to GaLV *env* gene. However, Stitz *et al.* disclose such a chimeric *env* sequence from MLV and GaLV in pseudotyped MLV vectors. See page 17, right column, the section under "Construction of chimeric *env* genes derived from GaLV and MLV." The lentiviral vectors exhibit a host cell range identical with that of MLV(GaLV) and MLV(10A1) vectors, which are known to enter cells either via the GaLV-receptor Glvr-1 (Pit-1) or via the amphotropic receptor Ram-1 (Pit-2) in addition to Glvr-1, respectively. See Abstract. The plasmid encodes the MLV-A env gene from molecular clone starin 4070A (page 19, right column, Materials and Methods).

Since the claimed sequences are derived from MLV *gag*, *pol*, and MLV-GaLV chimeric *env*, and Hu *et al.* and Stitz *et al.* disclose MLV *gag*, *pol*, and MLV-GaLV chimeric *env*, the claimed sequences, SEQ ID NO:1-5, must be inherently disclosed in Hu *et al.* and Stitz *et al.* Where Applicants claim a composition in terms of a characteristic not explicitly disclosed by the reference, a 103 rejection is proper (MPEP §2112). Patent owner's burden under the circumstances presented herein was described in *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977) as follows:

> Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. . . . Whether the rejection is based on 'inherency' under 35 U.S.C. §102, on 'prima facie obviousness' under 35 U.S.C. §103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior ad products (footnote omitted).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the plasmid vector of Hu *et al.* by substituting the GaLV *env* sequence with the chimeric *env* sequence from GaLV and MLV 10A1, as taught by Stitz *et al.* The skilled artisan would have been motivated to do so to improve gene transfer efficiency into important target cells such as human hematopoietic cells and peripheral blood leukocytes. There would have been a reasonable expectation of success, given that the modified Env exhibit cell tropism of GaLV and MLV-10A1, which is a broader host range, as taught by Stitz *et al.* Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim 8 is rejected under 35 U.S.C. §103(a) as being unpatentable over Hu *et al.* (US 7,101,541 B2) in view of Stitz *et al.* (2000), and further in view of Eglitis *et al.* (1995, IDS No. CH).

The instant invention is further limited to part of the *env* derived from the SEATO strain of GaLV.

The relevance of Hu *et al.* and Stitz *et al.* is set forth above. Neither reference discloses the SEATO strain. However, Eglitis *et al.* describe the SEATO strain of GaLV. See Abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the plasmid vector of Hu *et al.* by substituting the GaLV *env* sequence with the chimeric *env* sequence from GaLV and MLV 10A1, as taught by

Stitz *et al.*, and by using the GaLV from SEATO strain, as taught by Eglitis *et al.* The skilled artisan would have been motivated to do so to improve gene transfer efficiency into target cells. There would have been a reasonable expectation of success, given that the GaLV are primate-derived C-type retroviruses with a broad host range and that the SEATO strain replicates efficiently in 13 of 17 human cell lines tested and more than vectors packaged with MLV-A *env*, as taught by Eglitis *et al.* Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Remarks

No claim is allowable.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP §714.02 and §2163.06.

Contact Information

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Jeffrey Parkin, Ph.D.
Primary Examiner
22 September 2006